Author's response to reviews

Title: Autoadjusting- Continuous Positive Airway Pressure effect on serum Leptin levels in Obstructive Sleep Apnoea patients

Authors:

Marta Drummond (marta.drummond@gmail.com)
Joao C Winck (jcwinck@mail.telepac.pt)
Joao T Guimaraes (jtguimar@med.up.pt)
Ana C Santos (acsantos@med.up.pt)
Joao Almeida (malmeida@hsjoao.min-saude.pt)
Jose A Marques (jagosmarques@hotmail.com)

Version: 4 Date: 14 July 2008

Author's response to reviews: see over
Answers to Reviewer´s José M Gómez questions

Title: Autoadjusting-CPAP effect on serum Leptin levels in Obstructive Sleep Apnoea patients

Reviewer's report:

1) Question- Title and abstract. The authors should explain first the abbreviations as CPAP, OSA, APAP, BMI and change levels for concentrations.

Answer- We have explained all the abbreviations as you suggested and the leptin unit concentrations were also altered. (p.e see Title and Abstract)

2) Question- They state that leptin decrease after therapy but it is not true because the difference is no statistically significant and in the conclusion they state the opposite.

Answer- We have stated in the conclusion that “Short- and long-term APAP therapy produces a small and not significant reduction in plasma leptin levels”. So we do admit that APAP therapy does not have a significant effect on leptin serum levels.

3) Question- They also present the correlation between leptin and OSA, but where is this correlation in the results?

Answer- We have stated in the conclusions that “OSA patients show elevated leptin serum plasma levels”, according to the results and its comparison with the normal range “We found that those levels are clearly elevated in OSA patients (mean basal value=12.1±12.2 ng/mL; men normal range: 3.8±1.8 ng/mL) and we also could observe that “sixty percent of patients presented elevated basal leptin levels”, also after comparing with the normal range.
4) Question- Introduction. Line 6, twofold have to be corrected, and the text is very long.

Answer- The phrase is now: "It is known that every 10-Kg increment in body weight doubles OSA risk “(page 2, line 16).

5) Question- Material and Methods. Subjects, the authors have to explain in 4 line (AHI>20/h).

Answer- In the text instead of AHI appears Apnoea/Hypopnoea Index (page 4, line 12).

6) Question- Study procedures, BMI have to be described in methods.

Answer- In the new version we explain what is BMI (page 5, line 8)

7) Question- Results. Correct triglicerides, line 2.

Answer- The authors created a table (Table 4) with that information according to reviewer 2 suggestion, and the word is now corrected.

8) Question- Leptin 2nd line, leptin is elevated in relation to controls. Where are the controls?

Answer- We never stated that leptin levels in our patients group were greater than in controls. We just mention that leptin levels in OSA patients are greater that the considered normal range for men in our Lab.
By the previous comment it is obvious that we do not have a control group which is viewed in the discussion as a limitation of this study.
9) **Question**- Auto-CPAP, leptin decrease really?

**Answer**- We have clearly stated in the results and in the conclusions that “Leptin levels decrease after short and long-term APAP therapy were not statistically significant”.

10) **Question**- Discussion. 3th paragraph appear the normal range of leptin in normals; they should be placed in methods and results.

**Answer**- The normal range of leptin in men is now placed in methods and results, according to your suggestion (see page 5 line 22 and page 6 line 27).

11) **Question**- Tables. They should explain the abbreviations

**Answer**- All the abbreviations in tables are now explained according to your suggestion (see Tables 1 and 3).
Answers to Reviewer´s Ferran Barbé question

Minor essential revisions:

1) In “Abstract”, section “Materials and Methods” is presented a following time of 9 days and 6 months. However, in “Study Procedure” 4\textsuperscript{th} paragraph the following time is different this being one week and 6 months. It must be clarified.

Answer- In fact the second medical visit and the second leptin serum measurement were performed 9 days (mean value) after the APAP initiation, so we have changed one week for 9 days in the abstract.

2) In “Discussion” 5\textsuperscript{th} paragraph suggest that the leptin levels are mostly associated with obesity and not with OSAHS itself. Nevertheless, Barcelo et al. 2005 (1) (Figura 1) show significant difference in leptin levels between non-obese OSAHS patients and non-obese controls. The difference in leptin levels would be related to disease itself, being OSA the possible causative of the differences showed.
Due to, the lack of control group in the present work, that statement should be considered more profoundly.

Answer- As we discussed in our study “We found that leptin levels are clearly elevated in OSA patients but these levels did not correlate with OSA severity when considering confounders as obesity and fat distribution” but others did” as you also mentioned (our reference number 34).
So we have now included a new paragraph stating: «Moreover, in studies including a control group some authors (34) have shown significant difference in leptin levels between non-obese OSA patients and non-obese controls, being OSA the possible causative of the differences found.}
Discretionary Revisions:

1) The population characteristic described in “Results”, section “Habits and Comorbidities” could be presented in table including other important parameters like arterial hypertension values...

**Answer:** We have now included a new table (Table 4 Habits and comorbidities) and added new data about arterial blood pressure values in a new paragraph: “Arterial Hypertension (AH) was observed, according to 24-hour ambulatory blood pressure results, in 47.2% cases, being 2.8% nocturnal AH. The baseline mean overall blood pressure (BP), mean systolic BP and mean diastolic BP were, respectively, 101.95 mmHg, 134.98 mmHg and 83.17 mmHg”.

2) Leptin unit in article is referred as ug/L whereas in the bibliography it is usually presented like “ng/ml” although the number does not change, obviously.

**Answer:** For the sake of uniformity we have changed ug/L for ng/ml in all the manuscript (including tables).